APPENDIX 1
ROBUST SUMMARIES

I U C L I D

Data Set

Existing Chemical	:	ID: 101144
Producer related part		
Company	:	Epona Associates, LLC
Creation date	:	19.12.2005
Substance related part		
Company	:	Epona Associates, LLC
Creation date	:	19.12.2005
Status	:	
Memo	:	MOCA
Printing date	:	22.12.2005
Revision date	:	
Date of last update	:	22.12.2005
Number of pages	:	19
Chapter (profile)	:	Chapter: 2.1, 2.2, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.5, 4.1, 4.2, 4.3, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.8.1, 5.8.2
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 MELTING POINT

Value	:	= 102 - 107 °C
Sublimation	:	
Method	:	other
Year	:	2000
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data are taken from a secondary literature source (handbook)
Flag	:	Critical study for SIDS endpoint

19.12.2005 (2)

Value	:	= 110 °C
Sublimation	:	
Method	:	other
Year	:	1983
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction Data were obtained by modeling, SRC recommended value

19.12.2005 (56)

2.2 BOILING POINT

Value	:	= 378.9 °C at
Decomposition	:	
Method	:	other: calculation
Year	:	1988
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data were obtained by modeling, estimated by PCCHEM-PCGEMS, SRC recommended value
Flag	:	Critical study for SIDS endpoint

19.12.2005 (51)

2.4 VAPOUR PRESSURE

Value	:	= .0000133 hPa at 25 °C
Decomposition	:	
Method	:	
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 1.0 x 10E-5 mm Hg at 25 deg C
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
Flag	:	Critical study for SIDS endpoint

21.12.2005 (50)

Value	:	< 0 hPa at 25 °C

Decomposition	:	
Method	:	other (calculated)
Year	:	1988
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 1.32E-8 mm Hg at 25C Calc
Reliability	:	(2) valid with restrictions Data were obtained by modeling, estimated by PCCHEM-PCGEMS, SRC recommended value
19.12.2005		(51)
Value	:	< 0 hPa at 25 °C
Decomposition	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 2.86X10-7 mm Hg @ 25 deg C Calc
Reliability	:	(2) valid with restrictions Data were obtained by modeling
19.12.2005		(59)
Value	:	= .0000173 hPa at 60 °C
Decomposition	:	
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 1.3 x 10E-5 mm Hg at 60 deg C
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
21.12.2005		(43)
Value	:	= .00173 hPa at 60 °C
Decomposition	:	
Method	:	other (measured)
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 1.3X10-3 torr @ 60 deg C
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
21.12.2005		(1)
Value	:	= .0000466 hPa at 100 °C
Decomposition	:	
Method	:	
Year	:	1983
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 3.5 x 10E-5 mm Hg at 100 deg C
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
20.12.2005		(50)
Value	:	= .0000719 hPa at 120 °C
Decomposition	:	

Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Vapor pressure = 5.4 x 10E-5 mm Hg at 120 deg C
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data

20.12.2005 (43)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 3.61 - 3.9 at °C
pH value	:	-
Method	:	other (calculated)
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions EPA source document
Flag	:	Critical study for SIDS endpoint

19.12.2005 (27)

Partition coefficient	:	octanol-water
Log pow	:	= 3.94 at °C
pH value	:	
Method	:	other (calculated)
Year	:	1988
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Data were obtained by modeling, estimated by PCCHEM-PCGEMS, SRC recommended value

19.12.2005 (51)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 13.9 mg/l at 24 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	1986
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
Flag	:	Critical study for SIDS endpoint

19.12.2005 (61)

Solubility in	:	Water
Value	:	= 8.684 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	2005
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Water Solubility Estimate from Log Kow (WSKOW v1.41): Water Solubility at 25 deg C (mg/L): 8.684 log Kow used: 3.91 (expkow database) no-melting pt equation used
Reliability	:	(2) valid with restrictions Data were obtained by modeling

20.12.2005 (59)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .0000000000775166 cm³/(molecule*sec)
Degradation	:	= 50 % after .1 day(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2005
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Atmospheric Oxidation (25 deg C) [AopWin v1.91]: Hydroxyl Radicals Reaction: OVERALL OH Rate Constant = 77.5166 E-12 cm3/molecule-sec Half-Life = 0.138 Days (12-hr day; 1.5E6 OH/cm3) Half-Life = 1.656 Hrs Ozone Reaction: No Ozone Reaction Estimation
Reliability	:	(2) valid with restrictions Data were obtained by modeling
Flag	:	Critical study for SIDS endpoint

21.12.2005 (59)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm³
Rate constant	:	= .0000000000775 cm³/(molecule*sec)
Degradation	:	= 50 % after 5 hour(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	1993
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	t1/2 = 5 hours ; rate constant = 7.75X10-11 cu cm/molecule-sec at 25 deg C
Reliability	:	(2) valid with restrictions Data were obtained by modeling

20.12.2005 (38)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	> 1 year at 25 °C
t1/2 pH9	:	at °C

Deg. product	:	
Method	:	other: measurement
Year	:	1988
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions EPA source document
Flag	:	Critical study for SIDS endpoint

19.12.2005 (17)

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	> 800 year at 25 °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	other
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	4,4'-Methylenebis(2-chloroaniline) is not expected to undergo hydrolysis based on a hydrolysis half-life of greater than 800 years at pH 7 and 25 deg C.
Reliability	:	(2) valid with restrictions EPA source document

19.12.2005 (16)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other
Year	:	2005
Result	:	Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	9.87e-005	3.31	1000
Water	15.5	1.44e+003	1000
Soil	82.1	1.44e+003	1000
Sediment	2.42	5.76e+003	0

Persistence Time: 1.59e+003 hr

Reliability	:	(2) valid with restrictions Data were obtained by modeling
Flag	:	Critical study for SIDS endpoint

21.12.2005 (59)

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge

Concentration	:	100 mg/l related to Test substance related to
Contact time	:	28 day(s)
Degradation	:	= 0 (±) % after 28 day(s)
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	other
Year	:	1992
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	4,4'-Methylenebis(2-chloroaniline) is not expected to undergo biodegradation based on a screening test. 4,4'-Methylenebis(2-chloroaniline), present at 100 mg/liter, reached 0% of its theoretical BOD in 4 weeks using an activated sludge inoculum at 30 mg/liter and the Japanese MITI test.
Reliability	:	(2) valid with restrictions Japanese CITI studies are widely accepted as valid
Flag	:	Critical study for SIDS endpoint

20.12.2005 (10)

Type	:	aerobic
Inoculum	:	activated sludge
Concentration	:	2 mg/l related to Test substance related to
Contact time	:	
Degradation	:	= 0 (±) % after 42 day(s)
Result	:	
Deg. product	:	
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

STATIC SYSTEM:
BSA -- Biodegrades slow with acclimation
Rate: 10; 0; 0; 3; 1; 7; 6
Rate Units: % DEGRADATION
Oxygen Condition: AEROBIC
Analysis Method: GC
Incubation Time [Days]: 7
Test Chemical Conc. [ppm]: 2
Acclimation Period [Days]: 7; 14; 21; 28; 35; 42
Dissolved Organic Carbon: YEAST EXTRACT
Microbial Population: 10 (%)
Inoculum: ACTIVATED SLUDGE
Temperature [degrees C]: 25
Remarks: FLASKS SUBCULTURED FROM PREVIOUS WEEK

CONTINUOUS FEED SYSTEM
BFA -- Biodegrades fast with acclimation
Rate: 96; 96; 100; 94; 77; 100
Rate Units: % DEGRADATION
Oxygen Condition: AEROBIC
Continuous/Semi-Continuous Activated Sludge: c
Analysis Method: GC
Retention Time [Days]: 24
Test Chemical Conc. [ppm]: 2
Acclimation Period [Days]: 7; 14; 21; 28; 35; 42
Inoculum: ACTIVATED SLUDGE
Temperature [degrees C]: 25

Result : 4,4'-Methylenebis(2-chloroaniline) was not degraded after 6 weeks in a

static system in which 2 mg/l of the compound was seeded with sludge, incubated for 7 days, and the process repeated using cultures from the original system. However, when 4,4'-methylenebis(2-chloroaniline) containing water to a continuous feed activated sludge reactor, 96% of the chemical in the water was removed in 24 hours after 1 week of operation.

Reliability : (2) valid with restrictions
EPA source document

20.12.2005

(18)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= .61
Method	:	other
Year	:	2001
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Japanese MOE studies are widely accepted as valid
Flag	:	Critical study for SIDS endpoint

21.12.2005 (42)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= .92
Method	:	other
Year	:	2001
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Japanese MOE studies are widely accepted as valid
Flag	:	Critical study for SIDS endpoint

21.12.2005 (42)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	other: growth rate and biomass
Exposure period	:	72 hour(s)
Unit	:	mg/l
Method	:	other
Year	:	2001
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	Growth rate: 48 hr ECr50 > 1.9 mg/L; 48 hr NOEC = 1.4 Biomass: 72 hr ECb50 > 1.9 mg/L; 72 hr NOEC = 0.74
Reliability	:	(2) valid with restrictions Japanese MOE studies are widely accepted as valid
Flag	:	Critical study for SIDS endpoint

21.12.2005 (42)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 1140 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	1996
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data
Flag	:	Critical study for SIDS endpoint

19.12.2005 (28)

Type	:	LD0
Value	:	= 640 mg/kg bw
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	1996
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data

19.12.2005 (28)

Type	:	other
Value	:	
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	2000
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	In mice, poisoning is accompanied by adynamia, apathy, loss of appetite. Death occurs in 3 days. Manifestations of the toxic action in rats are not very pronounced and death occurs in 2 days. The LOEL for methemoglobinemia formation appears to be 83 mg/kg bw. Gross pathology examination revealed distention of the stomach and intestine, traces of blood in the urinary bladder, and pleural effusion in the thorax. Histology examination detected fine-drop adiposis of the liver, tiny foci of inflammatory infiltration, and circulatory disturbances in the visceral organs.
Reliability	:	(2) valid with restrictions

Source is peer-reviewed published data

20.12.2005 (49)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 5000 - mg/kg bw
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other
Year	:	1996
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(2) valid with restrictions Source is peer-reviewed published data

21.12.2005 (28)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium TA98 and TA100; Escherichia coli WP2uvrA
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	with
Result	:	positive
Method	:	other
Year	:	1994
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Results excerpted from ATSDR (1994) Toxicological Profile for 4,4'-Methylene-bis(2-chloroaniline) MBOCA. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry
Result	:	In vitro testing has provided clear and convincing evidence that MBOCA is mutagenic in the Salmonella typhimurium/mammalian microsome mutagenesis assay and that the mutagenic effect requires exogenous metabolic activation (Baker and Bonin 1981; Cocker et al. 1985; Dunkel et al. 1984; MacDonald 1981; Martire et al. 1981; McCann et al. 1975; Messerly et al. 1987; Rao et al. 1982). Although not all investigators used each tester strain, the general result is that MBOCA is mutagenic only in strains TA98 and TA100, at 250 µg/plate, with some inconsistency regarding strain TA98. MBOCA and its metabolites are not mutagenic in S.

typhimurium strains TA1535, TA1537, or TA1538. This suggests that the mutagenic effect of MBOCA metabolites in some bacteria is dependent on the plasmid pKM101; strains TA98 and TA100 contain this plasmid, but strains TA1535, TA1537, and TA1538 do not (Ames et al. 1975). This hypothesis is supported by the finding that S9-activated MBOCA is mutagenic in Escherichia coli strain WP2uvrA only in the presence of the plasmid pKM101 (Matsushima et al. 1981). The plasmid carries genes involved in an "errorprone" DNA repair system that introduces mutations as it removes DNA damage (Walker 1984). S9 derived from dog and human liver could activate MBOCA to a form mutagenic to strain TA100 but only in a protocol using a fluctuation assay (Cocker et al. 1985).

Most of MBOCA's mutagenic activity appears to be due to the N-hydroxy metabolite, which caused dose-dependent increases in mutations of S. typhimurium strains TA100 and TA98 in a pre-incubation assay using nonactivated doses of =5 µg/plate (Kuslikis et al. 1991). This metabolite is produced by several species, including dogs and humans (Butler et al. 1989; Chen et al. 1989; Morton et al. 1988). The mononitroso derivative appears to be direct-acting mutagen but is much less potent, causing a statistically significant revertant increase in the pre-incubation assay at the highest tested nontoxic dose (50 µg/plate). Neither the o-hydroxy nor the dinitroso derivatives were direct-acting mutagens at up to 50 or 500 µg/plate, respectively. Neither chemical was tested to cytotoxic levels (Kuslikis et al. 1991). N-acetylation is a deactivating step. Neither n-acetyl nor N,N-diacetyl derivatives were mutagenic in S. typhimurium in the absence of activation (Hesbert et al. 1985). In the presence of S9 activation, the mutagenic activity of the acetylated derivatives is less than that of the parent compound (Cocker et al. 1986; Hesbert et al. 1985).

Conclusion : In vitro testing has provided clear and convincing evidence that MBOCA is mutagenic in the Salmonella typhimurium/mammalian microsome mutagenesis assay and that the mutagenic effect requires exogenous metabolic activation

Reliability : (2) valid with restrictions
Source is peer-reviewed published data

Flag : Critical study for SIDS endpoint

21.12.2005 (3) (4) (5) (6) (11) (12) (13) (15) (21) (26) (29) (31) (32) (33) (37) (40) (45) (62)

Type : DNA damage and repair assay
System of testing :
Test concentration :
Cycotoxic concentr. :
Metabolic activation :
Result : positive
Method : other
Year : 1994
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : Results excerpted from ATSDR (1994) Toxicological Profile for 4,4'-Methylene-bis(2-chloroaniline) MBOCA. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry

Result : DNA adducts have been found following oral (Cheever et al. 1990; Kugler-Steigmeier et al. 1989; Segerback and Kadlubar 1992) and dermal (Cheever et al. 1990) administration of radiolabeled MBOCA to rats, following the incubation of radiolabeled MBOCA with explants of dog and human bladder urothelium (transitional cell epithelium) (Stoner et al. 1988) and incubation of rat DNA and radiolabeled N-hydroxy-MBOCA (Segerback and Kadlubar 1992). The level of binding increased with dose, but the increase was not linear. Considerable individual variation in binding levels, varying over at least a 10-fold range, was found in both dogs and humans. At least six adducts were found in dog bladder epithelium; four adducts

were found in human bladder epithelium, three of which appeared to be the same as those found in dogs. DNA adduct formation in dog bladder tissue is of particular note, since MBOCA has been found to cause bladder tumors in dogs (Stula et al. 1977).

Reliability : (2) valid with restrictions
Source is peer-reviewed published data

Flag : Critical study for SIDS endpoint
20.12.2005

(4) (8) (25) (48) (52) (53)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	other
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	positive
Method	:	other
Year	:	1994
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Results excerpted from ATSDR (1994) Toxicological Profile for 4,4'-Methylene-bis(2-chloroaniline) MBOCA. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry

Result : In vivo animal studies provide direct and indirect evidence that MBOCA is a mutagen; MBOCA metabolites were bound to DNA following oral (Cheever et al. 1990; Kugler-Steigmeier et al. 1989) or dermal (Cheever et al. 1990) exposure in rats. Small increases in the SLRL values were observed in D. melanogaster adults fed a 7.5millimolar MBOCA solution for 3 days (Vogel et al. 1981).

MBOCA induced gene mutations at the thymidine kinase (TK) locus in mouse lymphoma cells (Caspary et al. 1988; Myhr and Caspary 1988). Unscheduled DNA synthesis (UDS) was induced in HeLa cells (Martin and McDermid 1981), in rat primary hepatocytes at >10 µmol (McQueen et al. 1981; Mori et al. 1988; Williams et al. 1982) and in hamster (McQueen et al. 1981) and rabbit (McQueen and Williams 1987) hepatocytes. The concentration that tested positive in the mouse was 50 µmol (McQueen et al. 1981). Sensitivity to MBOCA showed species-specific variations: rat > mouse > hamster > rabbit (McQueen et al. 1981, 1983). Because hepatocytes have their own metabolic activation systems, no exogenous metabolic activation is needed. In assays using attachment independence as an end point, MBOCA, at concentrations near the LC50, transformed baby hamster kidney (Daniel and Dehnel 1981; Styles 1981), rat embryo (Dunkel et al. 1981; Traul et al. 1981), and Balb/3T3 cells (Dunkel et al. 1981).

Transformation assays have not been evaluated as thoroughly as some other genotoxicity assays. In an interlaboratory comparison, one laboratory found equivocal evidence that nonactivated MBOCA induced sister chromatid exchange in Chinese hamster ovary cells at a dose of 5.0 µg/mL. The response is considered equivocal because the dose-response curve was inconsistent. The result was not confirmed by the second laboratory. In the presence of S9 activation, positive results were obtained by one laboratory at 50 µg/mL. The other laboratory observed the beginning of a dose-response curve, but the high-dose (30 µg/mL) results

did not meet the testing laboratory's criterion for a positive response. In a chromosome aberration assay testing activated and nonactivated concentrations up to 5 and 30 µg/mL, respectively, neither laboratory found a positive result (Galloway et al. 1985). Another study (Perry and Thomson 1981) found no evidence of sister chromatid exchange at up to cytotoxic doses (100 µg/mL), but no doses were tested in the probable sensitive range (>10 and <100 µg/mL). Thus, MBOCA is clastogenic in some systems but not others.

In another study, MBOCA was classified as a clastogen on the basis of results from an in vivo micronucleus bone marrow assay (Katz et al. 1981). Evaluations using a two-phase micronucleus assay and intraperitoneal dosing of B6C3F1 hybrid mice were incomplete, but the results suggested that MBOCA is an in viva clastogen at doses of >32 mg/kg (Salamone et al. 1981) or 50% of the 1 LD50 (Katz et al. 1981). Results were inconclusive because of toxicity during the first phase of testing in which mice were dosed at 0 and 24 hours with 80% of the LD50 (51 mg/kg), and results were evaluated at 48 hours. In the second phase of testing, mice were dosed with 32 or 51 mg/kg and sampled 48 hours later, or in a separate test, dosed with 32 or 48 mg/kg and sampled 36 hours later. Results were negative at 32 mg/kg when sampled at 48 hours but positive at the same dose in a separate assay when sampled at 36 hours. Results were positive at the higher dose for both sampling times. Multiple sampling times were not performed in any assay (Salamone et al. 1981). In another study, results in the micronucleus test were negative at doses up to 50% of the LD50 (32 mg/kg) using CD-1 mice (dosing was done intraperitoneally at 0 and 24 hours and sampling at 30 hours) (Tsuchimoto and Matter 1981).

Conclusion : n vivo animal studies provide direct and indirect evidence that MBOCA is a mutagen.

Reliability : (2) valid with restrictions
Source is peer-reviewed published data

Flag : Critical study for SIDS endpoint
21.12.2005 (4) (7) (8) (14) (15) (19) (23) (25) (30) (34) (35) (36) (39) (41) (44) (47) (55) (57) (58) (60) (63)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

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APPENDIX 2
EPIWIN RESULTS

```
SMILES : Nc(c(cc(cl)Cc(ccc(N)c2CL)c2)CL)cl
CHEM   : Benzenamine, 4,4'-methylenebis 2-chloro-
CAS NUM: 000101-14-4
MOL FOR: C13 H12 CL2 N2
MOL WT : 267.16
------------------------------ EPI SUMMARY (v3.11) -------------------------
 Physical Property Inputs:
    Water Solubility (mg/L):   ------
    Vapor Pressure (mm Hg) :   ------
    Henry LC (atm-m3/mole) :   ------
    Log Kow (octanol-water):   ------
    Boiling Point (deg C)  :   ------
    Melting Point (deg C)  :   ------

 Log Octanol-Water Partition Coef (SRC):
    Log Kow (KOWWIN v1.67 estimate) =  3.47
    Log Kow (Exper. database match) =  3.91
       Exper. Ref:  Chem Inspect Test Inst (1992)

 Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.41):
    Boiling Pt (deg C):  404.79  (Adapted Stein & Brown method)
    Melting Pt (deg C):  156.63  (Mean or Weighted MP)
    VP(mm Hg,25 deg C):  3.93E-006  (Modified Grain method)
    MP  (exp database):  110 deg C
    BP  (exp database):  378.9 deg C

 Water Solubility Estimate from Log Kow (WSKOW v1.41):
    Water Solubility at 25 deg C (mg/L):  8.684
       log Kow used: 3.91 (expkow database)
       no-melting pt equation used
     Water Sol (Exper. database match) =  13.9 mg/L (24 deg C)
        Exper. Ref:  VOORMAN,R & PENNER,D (1986A)

 Water Sol Estimate from Fragments:
    Wat Sol (v1.01 est) =  4.5958 mg/L
    Wat Sol (Exper. database match) =  13.90
       Exper. Ref:  VOORMAN,R & PENNER,D (1986A)

 ECOSAR Class Program (ECOSAR v0.99g):
    Class(es) found:
       Aromatic Amines

 Henrys Law Constant (25 deg C) [HENRYWIN v3.10]:
   Bond Method :   3.29E-011  atm-m3/mole
   Group Method:   1.14E-011  atm-m3/mole
 Henrys LC [VP/WSol estimate using EPI values]:  1.591E-007 atm-m3/mole

 Probability of Rapid Biodegradation (BIOWIN v4.01):
    Linear Model         :  -0.1573
    Non-Linear Model     :   0.0003
 Expert Survey Biodegradation Results:
    Ultimate Survey Model:   1.8508  (months      )
    Primary Survey Model :   2.8463  (weeks       )
 Readily Biodegradable Probability (MITI Model):
    Linear Model         :  -0.3921
    Non-Linear Model     :   0.0006
```

```
Atmospheric Oxidation (25 deg C) [AopWin v1.91]:
  Hydroxyl Radicals Reaction:
     OVERALL OH Rate Constant =  77.5166 E-12 cm3/molecule-sec
     Half-Life =     0.138 Days (12-hr day; 1.5E6 OH/cm3)
     Half-Life =     1.656 Hrs
  Ozone Reaction:
     No Ozone Reaction Estimation

Soil Adsorption Coefficient (PCKOCWIN v1.66):
     Koc    :  1.353E+004
     Log Koc:  4.131

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v1.67]:
   Rate constants can NOT be estimated for this structure!

BCF Estimate from Log Kow (BCFWIN v2.15):
   Log BCF =  2.311  (BCF = 204.5)
      log Kow used: 3.91 (expkow database)

Volatilization from Water:
   Henry LC:  1.14E-011 atm-m3/mole  (estimated by Group SAR Method)
   Half-Life from Model River: 8.394E+007  hours   (3.498E+006 days)
   Half-Life from Model Lake : 9.158E+008  hours   (3.816E+007 days)

Removal In Wastewater Treatment (recommended maximum 99%):
   Total removal:              26.13  percent
   Total biodegradation:        0.29  percent
   Total sludge adsorption:    25.84  percent
   Total to Air:                0.00  percent

Level III Fugacity Model:
          Mass Amount    Half-Life    Emissions
           (percent)        (hr)        (kg/hr)
  Air       9.87e-005      3.31          1000
  Water     15.5           1.44e+003     1000
  Soil      82.1           1.44e+003     1000
  Sediment  2.42           5.76e+003     0
    Persistence Time: 1.59e+003 hr
```
